AMENDMENTS TO THE SPECIFICATION

Please replace the fourth paragraph, beginning on page 1 and ending on page 2, line 8, with the following amended paragraph:

The efficient delivery of DNA to cells *in vivo*, either for gene therapy or for antisense therapy, has been a major goal for some years. Much attention has concentrated on the use of viruses as delivery vehicles, for example adenoviruses for epithelial cells in the respiratory tract with a view to corrective gene therapy for cystic fibrosis (CF). However, despite some evidence of successful gene transfer in CF patients, the adenovirus route remains problematic due to inflammatory side-effects and limited transient expression of the transferred gene. Several alternative methods for *in vivo* gene delivery have been investigated, including studies using cationic surfactants. Gao,X *et al.* (1995) *Gene Ther.* **2**, 710-722 demonstrated the feasibility of this approach with a normal human gene for CF transmembrane conductance regulator (CFTR) into the respiratory epithelium of CF mice using amine carrying cationic lipids. This group followed up with a liposomal CF gene therapy trial which, although only partially successful, demonstrated the potential for this approach in humans (Caplen, NJ. *et al., Nature Medicine*, 1, 39-46, 1995). More recently other groups have investigated the potential of other cationic lipids for gene delivery, for example cholesterol derivatives (Oudrhiri,N *et al. Proc.Natl.Acad.Sci.* **94**, 1651-1656, 1997). This limited study demonstrated the ability of these cholesterol based compounds to facilitate the transfer of genes into epithelial cells ~~both *in vitro*~~ both *in vitro* and *in vivo*, thereby lending support to the validity of this general approach.

Please replace the third paragraph, beginning on page 5 and ending on page 6, line 21, with the following paragraph:

Another aspect of the invention relates to methods for using the spermine:peptide-based surfactant compounds. Such uses include facilitating the transfer of DNA or RNA polynucleotides, or analogs thereof, into a eukaryotic or prokaryotic ~~cell *in vivo*~~ cell *in vivo* or *in vitro*. These uses include facilitating transfection of polynucleotides to achieve an antisense knock-out effect, for gene therapy and genetic ~~immunisation~~ immunization (for the generation of antibodies) in whole organisms. Other uses include employing the compounds of the invention to facilitate the transfection of polynucleotides into cells in culture when such

transfer is required, in, for example, gene expression studies and antisense control experiments among others. The polynucleotides can be mixed with the compounds, added to the cells and incubated to allow polynucleotide uptake. After further incubation the cells can be assayed for the phenotypic trait afforded by the transfected DNA, or the levels of mRNA expressed from said DNA can be determined by Northern blotting or by using PCR-based quantitation methods for example the Taqman® method (Perkin Elmer, Connecticut, USA). Compounds of the invention offer a significant improvement, typically between 3 and 6 fold, in the efficiency of cellular uptake of DNA in cells in culture, compared with compounds in the previous art. In the transfection protocol, the gemini compound may be used in combination with one or more supplements to increase the efficiency of transfection. Such supplements may be selected from, for example:

(i) a neutral carrier, for example dioleyl phosphatidylethanolamine (DOPE) (Farhood, H., *et al* (1985) *Biochim. Biophys. Acta* 1235 289);

(ii) a complexing reagent, for example the commercially available PLUS reagent (~~Life Technologies Inc.~~ Invitrogen, Maryland, USA) or peptides, such as polylysine or polyornithine peptides or peptides comprising primarily, but not exclusively, basic amino acids such as lysine, ornithine and/or arginine. The list above is not intended to be exhaustive and other supplements that increase the efficiency of transfection are taken to fall within the scope of the invention.

Please replace the paragraph beginning on page 16, line 23, with the following paragraph:

Transfection studies were performed using the adherent cell line CHO-K1 (Puck et al. 1958). Complete medium consisted of MEM alpha medium supplemented with 10 % v/v foetal bovine serum and 1x L-Glutamine. All media and supplements were obtained from ~~Life Technologies~~ Invitrogen.

Please replace the paragragh beginning on page 16, line 27, with the following paragraph:

Stable transfected cell lines expressing β-galactosidase were generated by cotransfection of the plasmid pSV-β-Galactosidase Control Vector (Promega) with the plasmid Selecta Vecta-Neo (R & D Systems) in a 10:1 ratio. Following G418 (~~Life~~

~~Technologies~~ Invitrogen) selection (0.8 mg ml^{-1}), candidate cell lines were tested for β-galactosidase activity (β-Gal Reporter Gene Assay, chemiluminescent; Roche Diagnostics).

Please replace the paragraph beginning on page 17, line 5, with the following paragraph:

Cells were seeded into 96-well MTP plates (Beckton Dickinson) 16-18 hours prior to transfection at an approximate density of 1 x 10^4 cells per well. For transfection, 64ng of the luciferase reporter gene plasmid, pGL3-Control Vector (Promega) per well, was incubated with various concentrations of the spermine:peptide-based surfactant compounds and complexing agents. After 30 minutes incubation at RT, OPTI-MEM® medium (~~Life Technologies~~ Invitrogen) was added to the transfection mixture and the solution placed on the cells (final volume per well: 100 µl). Following a 3 hour or over night incubation at 37°C, the transfection solution was replaced with complete medium and the cells incubated further at 37°C. Reporter gene assays were performed according to the manufacturer's guidelines (Roche Diagnostics) approximately 48 hours post transfection. Luminescence was measured in a Packard TopCount NXT Microplate Scintillation and Luminescence Counter. For normalization purpose, β-galactosidase activity (β-Gal Reporter Gene Assay, chemiluminescent; Roche Diagnostics) was measured and luciferase activity per β-galactosidase activity was calculated.

Please replace paragraphs 1 and 2 on page 18, lines 4-12, with the following paragraphs:

Figure 1a and Figure 1b. General ~~sheme~~ scheme for synthesis of spermine:peptide-based surfactant compounds wherein the carbonyl groups (in this instance dodecanoyl) are linked to the spermine moiety by ~~amide~~ amine bonds. The final compound in Fig 1a is the first compound in Fig 1b.

Figure 2a and Figure 2b. General ~~sheme~~ scheme for synthesis of spermine:peptide-based surfactant compounds wherein the carbonyl groups (in this instance dodecanoyl) are linked to the spermine moiety by ~~amine~~ amide bonds. The final compound in Fig 2a is the first compound in Fig 2b.